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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/656,450 | 09/05/2003 | F. Charles Brunicardi | 60710-00002USC1 | 8472 |

24238 7590 11/16/2006

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| EXAMINER | |
|---|---|
| SGAGIAS, MAGDALENE K | |
| **ART UNIT** | **PAPER NUMBER** |
| 1632 | |

DATE MAILED: 11/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/656,450 | BRUNICARDI, F. CHARLES | |
| | Examiner | Art Unit | |
| | Magdalene K. Sgagias | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *119-139* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-139* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's arguments filed 9/2/06 have been fully considered but they are not persuasive. The amendment has been entered. Claims 119-139 are pending. Claims 1-118 are canceled.

Claims 119-139 are under consideration.

### *Claim Objections*

Claims 119, 120, 121, 124, 125, 126, 127, 132 and 136 objection to minor informalities is withdrawn.

### *Specification*

The disclosure objection to minor informalities is withdrawn.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 119-121, 123-129, 131-134, 136-139 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. U.S. 6,716,824. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims embrace treatment of pancreatic tumor cells in a subject comprising administering to a subject a nucleic acid vector with insulin promoter SEQ ID NO: 1 operatively coupled to a cytotoxic gene wherein the cytotoxic gene in expressed in a pancreatic tumor cell and a prodrug. The breadth of the scope of the claims recited in the instant application is very broad and includes any route of administration of the claimed vector and a prodrug and obviously encompasses the route of direct administration as embraced by the claims 1-3 of U.S. Patent No. U.S. 6,716,824. The conflicting claims have been patented.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 119, 124, 127, 132 and 136 rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn.

Claims 119-139 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons presented in the office action mailed 3/3/06.

Applicants argue the abstract of the instant application discloses that pancreatic adenocarcinoma (PDA) cells are pancreatic tumor cells that typically do not express insulin and in example 2 of the specification the in vivo delivery of RIP-tk in combination with GCV resulted in decrease in tumor burden in SCID mice thus, enabling the killing of a pancreatic tumor cell in a subject where the pancreatic tumor cell does not express insulin. Applicants argue description for treating a PDX-1 positive pancreatic tumor cells is provided in vitro and in vivo in example 2, thus in enabling treatment of PANC-1 cells in vivo the specification enables the treatment of a PDX-1 positive pancreatic tumor cell in a subject. Applicants further argue that enabling description for killing a pancreatic tumor cell that does not express insulin and for treating a PDX-1 positive pancreatic tumor cell also provides enablement for other pancreatic tumor cells types that may be targeted for ablation such as β-cell tumor cells and insulinomas. These arguments are not persuasive.

As discussed in the office action mailed 3/3/06 pages 8-13 applicants have not provided guidance to override the issue of unpredictability for treating any type of pancreatic carcinoma other than pancreatic adenocarcinoma by way of the claimed methods.

Applicants argue killing a PDX-1 positive tumor cell using an adenoviral vector delivery is enabled because in the field of gene therapy, adenoviral vector delivery of cytotoxic genes may be considered to have been reasonably well developed as of the filing date of the pending application and the protocol of **Hardy et al** (including citation in Appendix I) in combination with the description of the specification. Applicants further argue in the field of gene therapy basic technology fro the production of recombinant nucleic acid molecules was very well developed a of the filing date of the pending application and in view of the disclosure of producing a vector with an insulin promoter having SEQ ID NO: 2 operably linked to SEQ ID NO: 3 or 4 could be accomplished without undue experimentation. These arguments are not persuasive.

The breadth of the claims encompass in vivo methods of delivery being for purposes of gene therapy of killing a pancreatic tumor cell in a subject having a pancreatic tumor. For the reasons presented in the office action mailed 3/3/06, the rejection over methods of delivery in vivo are maintained as not being enabled because at the time of filing gene therapy was regarded by the art as being unpredictable without undue experimentation. The Hardy paper cited by the Applicant provides evidence for the construction of and production of highly enriched gutless adenovirus based vector preparation in very large quantities for gene therapy. However, the Hardy paper does not provide evidence to override the issue of unpredictability of administering to a subject having a pancreatic tumor a vector comprising said cytotoxic gene wherein the gene is expressed at sufficient levels and administering a prodrug to said subject resulting in killing a pancreatic tumor cell in a subject.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magdalene K. Sgagias whose telephone number is (571) 272-3305. The

examiner can normally be reached on Monday through Friday from 9:00 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram R. Shukla, can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Magdalene K. Sgagias, Ph.D.
Art Unit 1632

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630